REMARKS/ARGUMENTS

By this Amendment, claim 1 is amended. Claims 1-67 are pending.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2009/0163513 (Parthasaradhi Reddy et al.). Support for the claim amendments can be found throughout the Specification as filed. No new matter is added by this amendment.

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Allowable Subject Matter

The Examiner's indication of the allowability of claims 22-24 and 37-58 is gratefully acknowledged.

Rejection under 35 USC § 112 second paragraph

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

The Examiner argues that Applicants claim the conversion of compound(s) of formula (I) to its solvated form, however, it is not clear how the conversion is achieved from the compound to the solvated form.

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph "by providing clear warning to others as to what constitutes infringement of the patent". See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). MPEP 2173.02, MPEP 2173.02. In the instant case, the Specification demonstrates that the claimed method can produce a solvated form, see Example 4 (¶[0084]) which produces the hemihydrate and Example 5 (¶[0085]) which produces the monohydrate.

The Examiner argues that that formula (I) is not disclosed in claim 1, thus rendering the claim and claims depended therefrom indefinite.

However, claim 1 has been amended to clarify that the structure of the compound of formula (I) is shown in claim 1.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 103

Claims 1-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al, U.S. Patent Number 4,831,031 in view of Howard et al. This rejection is respectfully traversed.

The Examiner argues that Lowe '031, teach a process for preparing compounds of formula (I) which comprises reacting compounds of non-silylated formula (II) with compounds of formula (IV), citing the entire reference especially Example 16.

The Examiner admits that the difference between the instant process and that of Lowe '031 is that, Lowe '031 is silent on the use of a specific silylated compound., but argues that, from a reading of the specification, the silylated reactant (formula (III)) do not appear to provide any advantage to the current process and the compound produced in terms of bio-availability. The Examiner further argues that Howard et al., teach that the use of an analogous silylated compound for the making of ziprasidone is known and expected to succeed, citing the entire reference, especially Scheme 2.

The Examiner argues that the variables are merely optimization of variables, which are not patentable absent unexpected result due to these variables allegedly since the prepared compound is structurally and chemically the same as claimed.

The Examiner argues that at the time of filing this application, it would have been prima facie obvious to one of ordinary skill in the art to prepare ziprasidone and salts as disclosed by Lowe et al., with a reasonable expectation that the resulting product would be pure because Howard et al., discloses that ziprasidone can be prepared from an analogous silylated compound as disclosed by the reference (Scheme 2). Hence, one in possession of Lowe et al., and Howard et al., is in possession of the instant process absent a showing of unexpected results and/or properties.

However, the claims are patentable over the combination of the Lowe '031 patent and the Howard et al reference for the following reasons. The framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows: (A) Determining the scope and content of the prior art; and (B) Ascertaining the differences between the claimed invention and the prior art; and (C) Resolving the level of ordinary skill in the pertinent art. To establish prima

facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (*KSR v Teleflex*, 12 S.Ct. 1727, 1740 (US 2007)).

The claims are directed to a process for preparing ziprasidone or a pharmaceutically acceptable salt thereof; or a solvate or a hydrate thereof which comprises silylating 1-(1,2-benzisothiazol-3-yl)piperazine of the formula II with a silylating agent to form a compound of the formula III, and reacting the silyl compound of the formula III with a 5-(2-haloethyl)-6-chloro-oxindole compound of the formula IV in a solvent in the presence of a base to neutralize the hydrohalic acid, at about 400C to the reflux temperature of the solvent used to form the compound of formula I and optionally converting the compound of formula I into a pharmaceutically acceptable acid addition salt thereof, or a solvate or a hydrate thereof.

Here the combination of the Lowe '031 patent and the Howard et al. reference does not teach or suggest all the limitations of the claims, because, as the Examiner has indicated, none of the prior art teaches or suggests reacting a silylating compound, such as the silylated compound of clams 22-24 (i.e., the compound of form III). Accordingly, since the claims comprise a step of reacting a silylating compound, such as the compound of formula III with the compound of formula IV, the combination of the references does not teach or suggest reacting the compound of formula III to form ziprasidone.

Furthermore, there is no motivation for one of skill in the art to alter the methods of the '031 Lowe patent or the Howard reference to arrive at the claimed method, and no reasonable expectation of success. The Examiner argues that the motivation is that the resulting product would be pure because Howard et al., discloses that ziprasidone can be prepared from an analogous silylated compound as disclosed by the reference (Scheme 2). However, the combination of the '031 Lowe patent or the Howard reference does not teach or suggest all the claim limitations, specifically the combination does not teach or suggest reacting a silylating compound, such as the compound of formula III to form ziprasidone, and therefore, since the combination of the patents does not disclose or suggest these limitations, there is no motivation

to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 103

Claims 25-36 are rejected under 35 U.S.C. 1 03(a) as being unpatentable over Busch et al., (WO 03/070246) and Lowe et al., U.S. Patent Number 4,831 ,031 each taken alone. This rejection is respectfully traversed.

The Examiner argues that Busch et al., teach a process for preparing compounds of formula (I) which comprises reacting compound of formula (3) with compound of formula (4) obtain formula (I), citing the entire reference especially pages 15 and 16, Schemes 1 and 2.

The Examiner admits that the difference between the instant process and that of Busch is that Busch teaches the preparation and isolation of various intermediate compounds, and that Lowe et al., teaches that the use of various solvents such as amines (i.e., tertiary amines and carbonates) during the preparation of ziprasidone is known and, expected to succeed, citing Example 16. The Examiner argues that the preparation of a known compound (in this instant ziprasidone) is considered prima facie obvious when all the necessary reactants are known.

The Examiner argues that the solvents of claims 8, 9, 10, 13 and 14 and bases of claims 16 and 17 which are known and are obvious modifications well within the purview of the skilled artisan. The variables are merely optimization of variables, which are not patentable absent unexpected result due to these variables since the prepared compound is structurally and chemically the same as claimed herein.

The Examiner argues that it would have been prima facie obvious to one of ordinary skill in the art to prepare ziprasidone and salts as disclosed by Busch et al., and Lowe et al., with a reasonable expectation that the resulting product would be pure because each of the references discloses that ziprasidone can be prepared from the required reactants (compounds). Hence, one in possession of Busch et al., and Lowe et al., is in possession of the instant process absent a showing of unexpected results and/or properties. The process that is being claimed is a predictable and expected process.

The claims are directed to a process for preparing ziprasidone or a pharmaceutically acceptable salt thereof; or a solvate or a hydrate thereof which comprises silylating 1-(1,2-benzisothiazol-3-yl)piperazine of the formula II with a silylating agent to form a compound of

the formula III, and reacting the silyl compound of the formula III with a 5-(2-haloethyl)-6-chloro-oxindole compound of the formula IV in a solvent in the presence of a base to neutralize the hydrohalic acid, at about 400C to the reflux temperature of the solvent used to form the compound of formula I and optionally converting the compound of formula I into a pharmaceutically acceptable acid addition salt thereof, or a solvate or a hydrate thereof.

Here the combination of the Busch reference and the '031 Lowe patent does not teach or suggest all the limitations of the claims, because, as the Examiner has indicated, none of the prior art teaches or suggests reacting a silylating compound, such as the silylated compound of clams 22-24 (i.e., the compound of form III). Accordingly, since the claims comprise a step of reacting a silylating compound, such as the compound of formula III with the compound of formula IV, the combination of the references does not teach or suggest reacting the compound of formula III to form ziprasidone.

Furthermore, there is no motivation for one of skill in the art to alter the methods of the Busch reference and the '031 Lowe patent to arrive at the claimed method, and no reasonable expectation of success. The Examiner argues that the motivation is that the resulting product would be pure because each of the references discloses that ziprasidone can be prepared from the required reactants (compounds). However, the combination of the Busch reference and the '031 Lowe patent does not teach or suggest all the claim limitations, specifically the combination does not teach or suggest reacting a silylating compound, such as the compound of formula III to form ziprasidone, and therefore, since the combination of the patents does not disclose or suggest these limitations, there is no motivation to combine the references to reach these limitations, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

* * *

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.